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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/437,450	11/10/99	FREEDMAN J	1579-315

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EXAMINER	
PARAS JR,P	
ART UNIT	**PAPER NUMBER**
1632	8

DATE MAILED: 01/19/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/437,450	Applicant(s) FREEDMAN ET AL.	
	Examiner Peter Paras	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 4* is/are pending in the application.

4a) Of the above claim(s) *3* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-2 and 4, in Paper No. 7 is acknowledged. Claim 3 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 7.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, and 4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is directed to an isolated C. elegans gene that is modulated by cadmium. Claim 2 is directed to an isolated mRNA molecule encoded by the same gene. Claim 4 is directed to a transgenic C. elegans comprising any cadmium responsive gene. Note, the term "gene" is interpreted to encompass a genomic nucleotide sequence, which includes exons and introns.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the

filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed."Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1116.

While the specification provides adequate written description for the *mtl-2* gene with regard to *C. elegans* cadmium responsive genes, the specification fails to describe the other species within the genus of C. elegans cadmium responsive genes or corresponding full length cDNA sequences, and any and all transgenic *C. elegans* comprising any cadmium responsive gene encompassed in the claims with particularity to indicate that Applicants had possession of the claimed invention. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art **as of Applicants effective filing date**. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). In the instant case, the claimed embodiments of any and all C. elegans cadmium responsive genes, corresponding full length cDNA sequences, and any and all transgenic *C. elegans* comprising any and all cadmium responsive genes, lack a written description. The specification fails to describe

what genomic sequences or cDNA sequences [other than the mtl-2 gene] or any transgenic *C. elegans*, fall into this genus when and constructed and used as claimed, and it was unknown as of Applicants' effective filing date that any of these genes would be regulated by cadmium or if any of the transgenic *C. elegans* comprising any and all cadmium responsive genes would function as a biomonitor in response to cadmium. The skilled artisan cannot envision the detailed chemical structure of all of the encompassed *C. elegans* cadmium responsive genes or corresponding full length cDNA sequences, as well as the phenotypes of any and all transgenic *C. elegans* comprising any and all cadmium responsive genes, wherein the transgenic C. elegans is used as a biomonitor, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only the *mtl-2* gene meets the written description provision of 35 U.S.C. §112, first paragraph.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 1-2, and 4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a *C. elegans mtl-2* gene, does not reasonably provide enablement for any and all *C. elegans* genes (as well as their corresponding full length cDNAs) that are regulated by cadmium or for any and all transgenic C. elegans comprising any and all cadmium responsive genes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 1 is directed to an isolated C. elegans gene that is modulated by cadmium. Claim 2 is directed to an isolated mRNA molecule encoded by the same gene. Claim 4 is directed to a transgenic C. elegans comprising any cadmium responsive gene. Note, the term "gene" is interpreted to encompass a genomic nucleotide sequence, which includes exons and introns.

The specification teaches the nucleotide sequence of *mtl-2* gene and the nucleotide sequence of *mtl-2* cDNA,

The specification does not teach the nucleotide sequence of any and all *C. elegans* genes or corresponding full length cDNAs or any and all transgenic *C. elegans*,

comprising any cadmium responsive genes, and their corresponding phenotypes, wherein the transgenic C. elegans is used as a biomonitor.

The specification discusses the isolation and characterization of novel genes that are responsive to cadmium. While the specification provides partial cDNA sequences of contemplated genes, the specification does not provide any guidance or working examples which demonstrate how to obtain the full length cDNA sequence or the genomic sequence of any of the contemplated cadmium responsive genes. The specification fails to provide any working examples that demonstrate if any of the isolated cDNA sequences produce a protein. Furthermore, **fails** to provide **any** working examples or guidance that demonstrate a specific use for any of the contemplated cadmium responsive genes; also it is not clear how cadmium might modulate any of the contemplated genes. Without any teaching or guidance one of skill in the art would not reasonably know how to use any of the contemplated cadmium responsive genes.

With regard to the contemplated transgenic *C. elegans*, as the specification fails to provide any relevant teachings or guidance with regard to the production of a transgenic *C. elegans* as claimed, one of skill would not be able to rely on the state of the transgenic art for an attempt to produce transgenic *C. elegans* comprising any and all cadmium responsive genes. This is because the state of the art of transgenics is not a predictable art with respect to transgene behavior and the resulting phenotype. While the state of the art of transgenics is such that one of skill in the art would be able to produce transgenic animals comprising a transgene of interest; it is not predictable if the transgene would be expressed at a level and specificity sufficient to cause a particular

phenotype. For instance, the level and specificity of expression of a transgene as well as the resulting phenotype of the transgenic animal are directly dependent on the specific transgene construct. The individual gene of interest, promoter, enhancer, coding, or non-coding sequences present in the transgene construct, the specificity of transgene integration into the genome, for example, are all important factors in controlling the expression of a transgene in the production of transgenic animal which exhibits a resulting phenotype. This observation is supported by Wall (Theriogenology, 1996) who states that "[o]ur lack of understanding of essential genetic control elements makes it difficult to design transgenes with predictable behavior." See page 61, last paragraph. See also Houdebine (Journal of Biotechnology, 1994) who discloses that in the field of transgenics, constructs must be designed case by case without general rules to obtain good expression of a transgene (page 275, column 1, 1st paragraph); *e.g.*, specific promoters, presence or absence of introns, *etc.* As such guidance is lacking in the instant specification, it fails to feature any correlation between the over-expression of any cadmium responsive gene in a *C. elegans*, and, thus, a specific resulting phenotype such that the transgenic *C. elegans* is used as a biomonitor.

Therefore, in view of the quantity of experimentation necessary to isolate any and all cadmium responsive genes (and corresponding full length cDNAs) from *C. elegans*, the absence of working examples that demonstrate a use for any of the contemplated cadmium responsive genes, and the unpredictability of creating transgenic *C. elegans*, comprising any and all cadmium responsive genes with regard to a correlatable phenotype that is reproducible wherein the transgenic *C. elegans* are used as

biomonitors, it would have required undue experimentation for one of skill in the art to make and use the invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by Freedman et al (J. Biological Chemistry, 1993, 268(4): 2554-2564).

Claim 1 is directed to an isolated C. elegans gene that is modulated by cadmium. Claim 2 is directed to an isolated mRNA molecule encoded by the same gene.

Freedman et al teach the nucleotide sequence of the *mtl-2* gene, the cDNA sequence of the *mtl-2* gene, and an mRNA molecule of the *mtl-2* gene. See throughout entire document. Thus, the teachings of Freedman et al meet all of the instant claim limitations.

Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by Ishii et al (Neuron, 1992, 9(5): 873-881, **abstract**).

Claim 1 is directed to an isolated C. elegans gene that is modulated by cadmium. Claim 2 is directed to an isolated mRNA molecule encoded by the same gene. Note,

since claim 1 does not recite how the gene is specifically modulated by cadmium, it is inherent that high levels of cadmium can modulate any *C. elegans* gene.

Ishii et al teach the isolation, cloning, and sequencing (both the genomic and cDNA sequences) of the C. elegans gene, unc-6. Thus, the teachings of Ishii et al meet all of the instant claim limitations.

Conclusion

No claims are allowed. Claim 4 is free of the prior art of record because the prior art of record does not teach or suggest a transgenic C. elegans comprising any cadmium responsive gene. Claim 4 however is subject to other rejections.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Peter Paras, Jr., whose telephone number is 703-308-8340. The examiner can normally be reached Monday-Friday from 8:30 to 4:30 (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen Hauda, can be reached at 703-305-6608. Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703)308-4242 and (703)305-3014.

Inquiries of a general nature or relating to the status of the application should be directed to Kay Pinckney whose telephone number is (703) 305-3553.

Peter Paras, Jr.

Art Unit 1632

JILL D. MARTIN
PATENT EXAMINER
AU 1632